

*Citation for published version:*

Chapman, R, Lawrence, R, Williams, J & Bull, S 2017, 'Formyloxyacetoxypheylmethane as an *N*-Formylating Reagent for Amines, Amino Acids, and Peptides', pp. 4908-4911. <https://doi.org/10.1021/acs.orglett.7b02382>

*DOI:*

[10.1021/acs.orglett.7b02382](https://doi.org/10.1021/acs.orglett.7b02382)

*Publication date:*

2017

*Document Version*

Peer reviewed version

[Link to publication](#)

## University of Bath

### Alternative formats

If you require this document in an alternative format, please contact:  
[openaccess@bath.ac.uk](mailto:openaccess@bath.ac.uk)

#### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

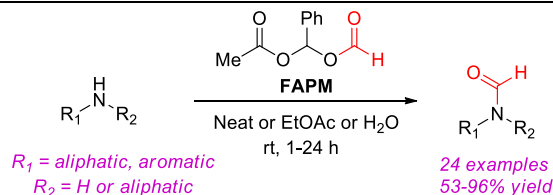
#### Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

# Formyloxyacetoxyphenylmethane as an *N*-Formylating Reagent for Amines, Amino Acids and Peptides

Robert. S. L. Chapman,<sup>‡</sup> Ruth Lawrence,<sup>‡</sup> Jonathan M. J. Williams and Steven. D. Bull\*

Department of Chemistry, University of Bath, Bath, BA2 7AY, UK.



**ABSTRACT:** Formyloxyacetoxyphenylmethane is a stable, water-tolerant, *N*-formylating reagent for primary and secondary amines that can be used under solvent-free conditions at room temperature to prepare a range of *N*-formamides, *N*-formyl-anilines, *N*-formyl- $\alpha$ -amino-acids, *N*-formyl-peptides and an isocyanide.

*N*-Formylation reactions of primary and secondary amines are important transformations in organic chemistry, because they provide direct access to the highly versatile formamide group.<sup>1</sup> Highlighting their synthetic utility, *N*-formyl derivatives can be used as precursors for the synthesis of formamidines,<sup>2</sup> ureas,<sup>3</sup> carbamates,<sup>3</sup> aryl amides,<sup>4</sup> isocyanates,<sup>5</sup> nitriles<sup>6</sup> and isocyanides.<sup>7</sup> Consequently, they have often been used as intermediates for the synthesis of pharmaceuticals.<sup>8</sup> Alternatively, the *N*-formyl group may be used as a protecting group for peptide synthesis,<sup>9</sup> whilst many naturally occurring formamides exhibit important medicinal and biological activities.<sup>10</sup> The formamide moiety is also present in pharmaceuticals, including Leucovorin (chemotherapeutic),<sup>11a</sup> Formoterol (asthma)<sup>11b</sup> and Orlistat (anti-obesity).<sup>11c</sup>

Due to their importance, a number of *N*-formylating reagents for primary and secondary amines have been developed,<sup>1</sup> including the use of formic acid,<sup>12a</sup> formic acid in the presence of coupling reagents (e.g. DCC),<sup>12b</sup> acetic formic anhydride,<sup>12c</sup> formate esters,<sup>12d</sup> formamides,<sup>12e</sup> trialkylorthoformates,<sup>12f</sup> enol formates,<sup>12g</sup> ammonium formate,<sup>12h</sup> and *N*-formyl-benzotriazole.<sup>12i</sup> However, many of these reagents are only moderately reactive towards sterically hindered or electronically deactivated amines, often requiring elevated temperatures, extended reaction times or the use of excess reagent for their *N*-formylation reactions to proceed to completion.<sup>1</sup> A number of these formylating reagents are also susceptible to hydrolysis, whilst some reagents can decompose to liberate hazardous by-products (e.g. C=O).<sup>1</sup> Given these limitations, a number of catalytic *N*-formylation protocols have also been developed that employ *N*-formyl donors in combination with acid catalysts, Lewis acids, organocatalysts, metal catalysts and biocatalysts.<sup>13</sup>

Given the limitations of using many *N*-formylating reagents under catalyst free conditions, we now report herein that formyloxyacetoxyphenylmethane (FAPM) **5** can be used as a bench-stable formylating reagent for primary/secondary amines under solvent-free conditions at room temperature. Importantly, the stability of FAPM **5** towards hydrolysis, enables it to be used

as a catalyst free *N*-formylating reagent for  $\alpha$ -amino acids and peptides in aqueous based solvent systems.

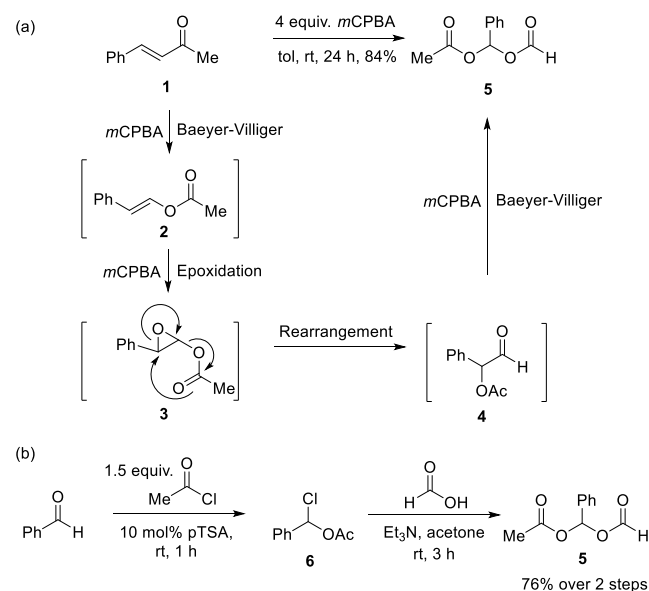
As part of investigations into the Baeyer-Villiger oxidation reactions of  $\alpha,\beta$ -unsaturated ketones, we found that treatment of benzylidene acetone **1** with 4 equiv. of *meta*-chloroperoxybenzoic acid (*m*CPBA) in toluene for 24 h gave FAPM **5** in 84% isolated yield (Scheme 1a).<sup>14</sup> In this remarkable one-pot 4-step reaction, benzylidene acetone **1** first undergoes an *m*CPBA mediated Baeyer-Villiger reaction to afford enol acetate **2**, whose electron-rich alkene bond is then epoxidised by a second equivalent of *m*CPBA to afford epoxy-acetate **3**. This unstable epoxy-acetate **3** then undergoes intramolecular rearrangement to afford aldehyde **4**, which then undergoes a further *m*CPBA mediated Baeyer-Villiger reaction to afford FAPM **5**. The formation of intermediates **2** and **4** in this oxidation reaction were confirmed by <sup>1</sup>H NMR spectroscopic analysis of a series of control reactions that were carried out using fewer equivalents of *m*CPBA over shorter periods of time (see SI for details).<sup>15</sup>

A second route to FAPM **5** was also developed using a variant of a protocol previously developed by Raphaeli and coworkers for the synthesis of non-symmetric acyloxyalkyl esters.<sup>16</sup> This involved treatment of benzaldehyde with 1.5 equiv. of acetyl chloride in the presence of a catalytic amount of *para*-toluene sulfonic acid to afford  $\alpha$ -chlorobenzyl acetate **6**,<sup>17</sup> that was subsequently reacted with formic acid and Et<sub>3</sub>N in acetone to afford FAPM **5** in 76% yield (Scheme 1b).<sup>18</sup>

FAPM **5** proved to be a bench-stable liquid that could be stored at room temperature under nitrogen for up to 6 months without decomposition. We reasoned that FAPM **5** might act as a selective *N*-formyl donor for amines, which was confirmed by reacting 1.5 equiv. of FAPM **5** with 1 equiv. of benzylamine **7a** in THF at rt for 4.5 h to give *N*-formyl-benzylamine **8a** and imine **9in** 90% and 10% conversion respectively (Table 1, entry 1). Importantly, <sup>1</sup>H NMR spectroscopic analysis revealed no evidence of any *N*-acetyl-benzylamide having been formed *via* competing *N*-acyl transfer from FAPM **5**. Mechanistically, we propose that

benzylamine **10a** attacks the reactive formyl group of FAPM to irreversibly afford formamide **8a**,

**Scheme 1.** Syntheses of formyloxyacetoxyphenylmethane **5** via: (a) *m*CPBA mediated oxidation reaction of benzylidene acetone **1**. (b) Nucleophilic attack of formic acid on  $\alpha$ -chlorobenzyl acetate **6**.



with benzaldehyde and acetic acid being generated as by-products. Unwanted formation of imine **9** then occurs through acid catalyzed reaction of benzylamine **7a** with the benzaldehyde by-product. A solvent screen was carried out with the aim of identifying conditions that would suppress formation of imine **9**. Use of ethanol and 1,4-dioxane (Table 1, entries 2-3) also afforded significant amounts of the unwanted imine **9** by-product (8-12%). Carrying out the *N*-formylation reaction in MeCN (Table 1, entry 4) gave reduced amounts of imine (4%), whilst CH<sub>2</sub>Cl<sub>2</sub>, toluene and EtOAc (Table 1, entries 5-7) gave excellent conversion to *N*-formyl-benzylamine **8a** with only trace amounts of imine **9** ( $\leq 2\%$ ) being formed. Since imine formation is potentially reversible, a series of *N*-formylation reactions were carried out in mixed aqueous solvents, in the hope that the presence of bulk water would perturb the reaction equilibrium away from imine formation. Gratifyingly, use of 1:1 mixtures of THF : H<sub>2</sub>O, MeCN : H<sub>2</sub>O and 1,4-dioxane : H<sub>2</sub>O (Table 1, entries 8-10) gave good conversions to *N*-formyl-benzylamine **8a**, with  $\leq 1\%$  of imine **9** being formed in each case. The tolerance of FAPM **5** towards hydrolysis in aqueous systems was confirmed by carrying out an *N*-formylation reaction in water,<sup>19</sup> with 1.5 equiv. of FAPM **5** resulting in complete conversion of benzylamine to *N*-formyl-benzylamine **8a** (Table 1, entry 11). Finally, FAPM **5** could also be used under solvent free conditions (Table 1, entry 12), resulting in clean *N*-formylation of benzylamine, with only 2% of imine **9** being produced.<sup>20</sup>

<sup>1</sup>H NMR spectroscopic analysis of the *N*-formylation reaction of benzylamine in d<sub>8</sub>-toluene revealed that complete consumption of benzylamine **7a** occurred after 1 h. Analysis after 15 min revealed the presence of a 87 : 13 mixture of formamide **8a** : imine **9**, which subsequently equilibrated to a 99 : 1 mixture of formamide **8a** : imine **9** after 1 hr. With this information in hand, we employed 1.5 equiv. of FAPM to *N*-formylate a range of sixteen primary and secondary amines **7a**- to afford a series of *N*-formamides **8a-p** in 53-96% yield after chromatographic purification (Scheme 2). Most of these *N*-formylation reactions were

carried out under solvent-free conditions by dissolving the amine in neat FAPM and stirring at rt, followed by purification by silica chromatography. In those cases where the parent amine was insoluble in FAPM **5**, then EtOAc was employed as a cosolvent to afford a homogeneous reaction mixture. *N*-Formylation reactions of primary aliphatic amines proved particularly facile; typically affording their corresponding formamides **8a-e** in good to excellent yields (81-95%). Pleasingly, amines containing acid sensitive functionalities, such as furan and dimethyl acetal were well tolerated, affording formamides **8b** and

**Table 1.** Solvent screen to optimize the *N*-formylation reaction of benzylamine with FAPM **5**

Entry	Solvent	Formamide <b>8a</b>	Imine <b>9</b>
1	THF	90	10
2	EtOH	88	12
3	Dioxane	92	8
4	MeCN	96	4
5	CH <sub>2</sub> Cl <sub>2</sub>	100	-
6	Toluene	100	-
7	EtOAc	98	2
8	THF : H <sub>2</sub> O (1 : 1)	99	1
9	MeCN : H <sub>2</sub> O (1 : 1)	100	-
10	Dioxane : H <sub>2</sub> O (1 : 1)	99	1
11	H <sub>2</sub> O	100	-
12	Neat	98	2

Product ratios determined from integrals of diagnostic resonances for **8a** and **9** in <sup>1</sup>H NMR spectra of crude reaction products.

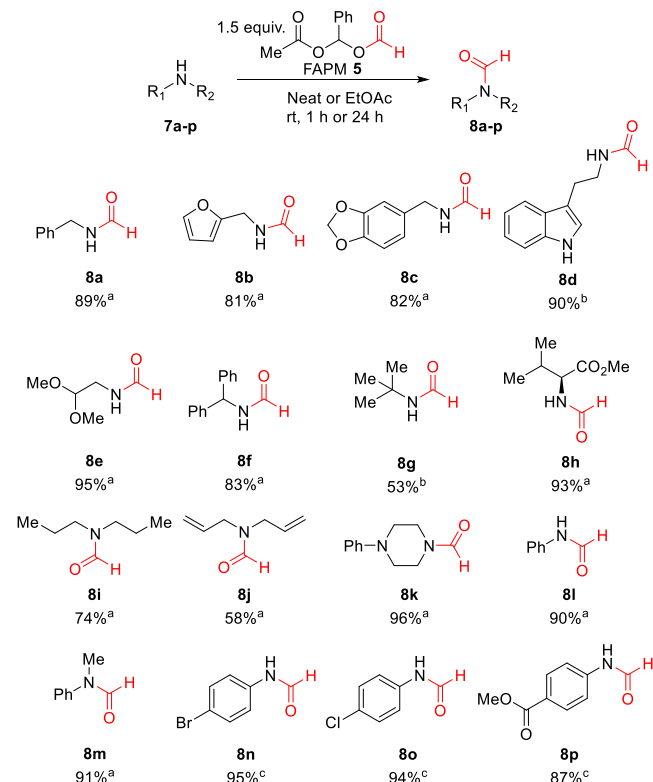
**8e** in 95% and 85% yields respectively. FAPM **5** reacted exclusively with the primary amine functionality of tryptamine to afford formamide **8d** in 90% yield. Whilst the formamide **8f** of sterically congested benzhydrylamine was formed in good 83% yield, formylation of *tert*-butylamine gave *N*-formamide **8g** in only 53% isolated yield, arising from losses during reaction work-up due to its volatility. (*S*)-Valine methyl ester afforded *N*-formamide **8h** in an excellent 93% yield, with no evidence of any racemization having occurred. Acyclic and cyclic secondary amines were also formylated using FAPM **5**, with moderate to excellent 58-96% yields of *N*-formamides **8i-k** being isolated. Pleasingly, electron-deficient aniline and its secondary *N*-methyl derivative gave their corresponding formamides **8l-m** in excellent 90% and 91% yields respectively. However, formylation of anilines containing deactivating halogen or ester groups required extended reaction times of 24 h for their corresponding *N*-formamides **8o-p** to be formed in 87-95% yields respectively.

Alternative work-up procedures were then developed to allow for these *N*-formylation reactions to be carried out on-scale, without the need for chromatographic purification. When the desired formamide product was crystalline, or a high boiling oil, then the acetic acid and benzaldehyde by-products could be removed by fractional distillation *in vacuo*. For more volatile formamides, purification could be achieved by first extracting the crude reaction product with NaHCO<sub>3(aq)</sub> to remove acetic acid, followed by extraction with NaHSO<sub>3(aq)</sub> to remove benzaldehyde. This affords a crude product containing the formamide that is then purified by recrystallisation or fractional distillation as required (See SI for details).

Although several reagents have been developed for the *N*-formylation of amino ester derivatives,<sup>21</sup> extension of these

methods to unprotected  $\alpha$ -amino acids has not been widely reported. This is due to the instability of many formylating reagents towards hydrolysis in aqueous media and the insolubility of  $\alpha$ -amino acids in non-aqueous solvents. Currently, *N*-formyl- $\alpha$ -amino acids are most commonly prepared via treatment of the parent  $\alpha$ -amino acids with a large excess of  $\text{Ac}_2\text{O}$  and formic acid (via formation of formyl acetate *in situ*), which often requires forcing conditions and/or extended reaction times.<sup>22</sup> *N*-formylation of  $\alpha$ -amino acids using formic acid in water has been reported, however this protocol requires Oxyma as a stoichiometric coupling reagent.<sup>22</sup> Given the observed stability of FAPM in aqueous solvents, a range of six L-amino acids **10a-f** were treated with 1.5 equiv. of FAPM in water containing 5 equiv. of  $\text{NaHCO}_3$  as a base, which resulted in 80–85% conversion to their corresponding formamides **11a-f** after 16 h. However, we subsequently found that modifying these formylation reactions, by incorporating addition of a second portion of FAPM **5** (1.5 equiv.) after 8 h, resulted in complete consumption of each  $\alpha$ -amino acid, giving *N*-formyl-amino acids **11a-f** in good to excellent 71–89% isolated yields, with no racemization having occurred (Scheme 3).

**Scheme 2:** FAPM **5** as an *N*-formylating reagent for the synthesis of *N*-formamides **8a-p**



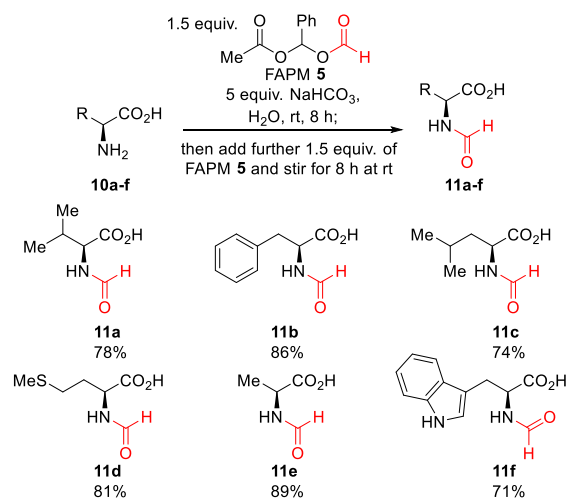
(a) Reaction conditions: 2 mmol of amine, 1.5 equiv. FAPM **5**, 1 h, rt. (b) Reaction conditions: 2 mmol of amine, 1.5 equiv. FAPM **5**, EtOAc, 1 h, rt. (c) Reaction conditions: 2 mmol of amine, 1.5 equiv. FAPM **5**, EtOAc, rt, 24 h.

*N*-Formylmethionine-leucyl-phenylalanine (f-MLP) **14** is a chemotactic *N*-formyl-tripeptide that is a potent chemoattractant for leukocytes and a macrophage activator that is involved in triggering the innate immune response towards bacterial pathogens,<sup>24</sup> that was chosen as a suitable target to test the utility of FAPM for the *N*-formylation of peptidic substrates. The parent tripeptide ester **12** was treated with 1.5 equiv. of FAPM in EtOAc for 5 h to afford formamide **13** in 87% yield, which was then hydrolysed using  $\text{NaOH}/\text{MeOH}$  to afford f-MLP **14** in 93% yield (Scheme 4a). Similarly, a decapeptide with the sequence Ac-

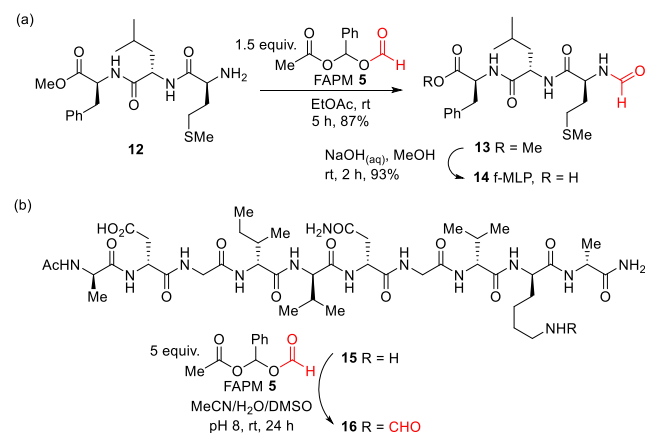
ADGIVNGVKA- $\text{NH}_2$  **15** containing *N*-acetamide and C-primary amide termini, was reacted with 5 equiv. of FAPM in a mixture of  $\text{MeCN}/\text{H}_2\text{O}$  (pH 8.0) containing a few drops of DMSO. This resulted in *N*-formylation of the free  $\omega$ -amino group of its lysine residue affording *N*-formyl-decapeptide **16**, as confirmed from HRMS analysis (Scheme 4b).

Formamides are often employed for the synthesis of isocyanides,<sup>7</sup> and so we investigated whether FAPM **5** could be used to develop a stepwise 'one-pot' protocol to directly convert an amine into its corresponding isocyanide. 4-Bromoaniline **7n** and FAPM **5** (1.5 equiv.) were stirred in  $\text{CH}_2\text{Cl}_2$  at rt for 24 h to afford its corresponding formamide **8n** *in situ* (confirmed by  $^1\text{H}$  NMR spectroscopic analysis). Sequential dropwise addition of diisopropylamine (4 equiv.) and  $\text{POCl}_3$  (1.2 equiv.) to this solution of formamide **8n** in  $\text{CH}_2\text{Cl}_2$  at  $0^\circ\text{C}$ , followed by stirring at  $0^\circ\text{C}$  for 2 h and rt for 4 h, gave 1-bromo-4-isocyanobenzene **17** in 74% yield over two steps (Scheme 5).

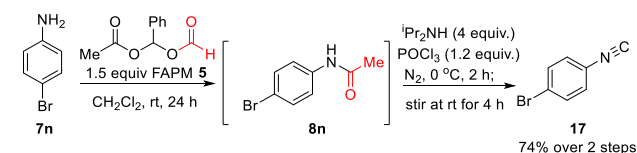
**Scheme 3:** FAPM **5** as an *N*-formylating reagent for the synthesis of *N*-formyl- $\alpha$ -amino acids **11a-f**.



**Scheme 4:** FAPM **5** for the synthesis of: (a) *N*-formylmethionyl-leucyl-phenylalanine (f-MLP) **14**; (b) *N*-formyl-decapeptide **16**



**Scheme 5:** FAPM **5** for the one-pot synthesis of isocyanide **17**



In conclusion, two practical syntheses of formyloxycetoxyphe-nylmethane **5** have been developed and its use as a water toler-

ant *N*-formylating reagent for primary and secondary amines under solvent-free conditions demonstrated. Its potential as a reagent for the synthesis of *N*-formyl- $\alpha$ -amino acids and *N*-formyl-peptides in aqueous systems has been established and it has also been used as an *N*-formylating reagent in a one pot protocol to convert an aniline into its corresponding isocyanide.

## ASSOCIATED CONTENT

Complete experimental procedure and relevant spectra ( $^{13}\text{C}$  and  $^1\text{H}$  NMR spectra) for all compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>

## AUTHOR INFORMATION

### Corresponding Author

\*E.mail:s.d.bull@bath.ac.uk

### Author Contributions

‡These authors contributed equally.

### Notes

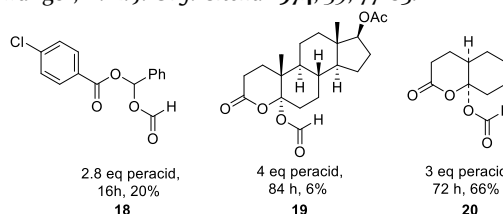
The authors declare no competing financial interest.

## ACKNOWLEDGMENT

We thank the University of Bath, EPSRC and the Centre for Doctoral Training in Sustainable Chemical Technologies (EP/L016354/1) for funding. We would like to thank Dr Jody Mason for donating a sample of decapeptide **15** that was prepared using conventional solid-phase peptide synthesis.

## REFERENCES

- Gerack, C. J.; McElwee-White, L. *Molecules* **2014**, *19*, 7689-7713.
- Han, Y.; Cai, L. S. *Tetrahedron Lett.* **1997**, *38*, 5423-5426.
- Faraj, M. K. *Synthesis of isocyanate precursors from primary formamides*, U.S. Patent 5,686,645, **1997**.
- Jo, Y.; Ju, J.; Choe, J.; Song, K. H.; Lee, S. J. *Org. Chem.* **2009**, *74*, 6358-6361.
- Fu, P. P.; Boyer, J. H. *J. Chem. Soc. Perkin Trans 1* **1974**, 2246-2250.
- Arlt, D.; Klein, G. *Preparation of nitriles from formamides*, U.S. Patent 4419297, **1983**.
- Obrecht, R.; Herrmann, R.; Ugi, I. *Synthesis* **1985**, 400-402.
- Jackson, A.; Meth-Cohn, O. *J. Chem. Soc. Chem. Commun.* **1995**, 1319.
- Yamashiro, D.; Li, C. H. *J. Org. Chem.* **1973**, *38*, 2594-2597.
- Wright, A. D.; Lang-Unnasch, N. *J. Nat. Prod.* **2009**, *72*, 492-495.
- (a) Machover, D. *Cancer* **1997**, *80*, 1179-1187. (b) Hett, R.; Fang, Q. K.; Gao, Y.; Wald, S. A.; Senanayake, C. H. *Org. Process Res. Dev.* **1998**, *2*, 96-99. (c) Ma, G.; Zancanella, M.; Oyola, Y.; Richardson, R. D.; Smith, J. W.; Romo, D. *Org. Lett.* **2006**, *8*, 4497-4500.
- (a) Jung, S. H.; Ahn, J. H.; Park, S. K.; Choi, J. K. *Bull. Korean Chem. Soc.* **2002**, *23*, 149-150. (b) Tornesello, A. L.; Sanseverino, M.; Buonaguro, F. M. *Molecules* **2016**, *21*, 736-742; (c) Strazzolini, P.; Giumanini, A. G.; Cauci, S. *Tetrahedron* **1990**, *46*, 1081-1081. (d) Christensen, S. B.; Hansen, A. M.; Franzky, H. J. *Peptide Sci.* **2017**, *23*, 410-415. (e) Cochet, T.; Bellosta, V.; Greiner, A.; Roche, D.; Cossy, J. *Synlett* **2011**, 1920-1922. (f) Kaboudin, B.; Khodamorady, M. *Synlett* **2010**, 2905-2907. (g) Neveux, M.; Bruneau, C.; Digneuf, P. H. *J. Chem. Soc. Perkin Trans 1* **1991**, 1197-1199. (h) Reddy, P. G.; Kumar, G. D. K.; Baskaran, S. *Tetrahedron Lett.* **2000**, *41*, 9149-9151. (i) Katritzky, A. R.; Chang, H. X.; Yang, B. Z. *Synthesis* **1995**, 503-505.
- (a) Brahmachari, G.; Laskar, S. *Tetrahedron Lett.* **2010**, *51*, 2319-2322. (b) Nguyen, T. B.; Sorres, J.; Tran, M. Q.; Ermolenko, L.; Al-Mourabit, A. *Org. Lett.* **2012**, *14*, 3202-3205. (c) Lei, M.; Ma, L.; Hu, L. *Tetrahedron Lett.* **2010**, *51*, 4186-4188. (d) Habibi, D.; Nasrollahzadeh, M.; Shebekhtari, H. *J. Mol. Catal. A* **2013**, *378*, 148-155. (e) Kim, J. G.; Jang, D. O. *Synlett* **2010**, 2093-2096. (f) Deutsch, J.; Eckelt, R.; Kockritz, A.; Martin, A. *Tetrahedron* **2009**, *65*, 10365-10369. (f) Sonawane, R. B.; Rasal, N. K.; Jagtap, S. V. *Org. Lett.* **2017**, *19*, 2078-2081. (g) Patre, R. E.; Mal, S.; Nilkanth, P. R.; Ghorai, S. K.; Deshpande, S. H.; El Qacemi, M.; Smejkal, T.; Pal, S.; Manjunath, B. N. *Chem. Commun.* **2017**, *53*, 2382-2385. (h) Hosseini-Sarvari, M.; Sharghi, H. *J. Org. Chem.* **2006**, *71*, 6652-6654. (h) Allen, C. L.; Atkinson, B. N.; Williams, J. M. J. *Angew. Chem. Int. Ed. Engl.* **2012**, *51*, 1383-1386. (i) Mamani, L.; Sheykhan, M.; Heydari, A.; Faraji, M.; Yamini, Y. *Appl. Cat. A* **2010**, *377*, 64-69.
- For previous reports where peracid mediated Baeyer-Villiger reactions of  $\alpha,\beta$ -unsaturated ketones gave mixtures of products containing formyl-acylals **18-20**, see: (a) Formyl-acylal **18**: Baures, P. W.; Eggleston, D. S.; Flisak, J. R.; Gombatz, K.; Lantos, I.; Mendelson, W.; Remich, J. J. *Tetrahedron Lett.* **1990**, *31*, 6501-6504. (b) Formyl-acylal **19**: Gorodetsky, M.; Danieli, N.; Mazur, Y. *J. Org. Chem.* **1967**, *32*, 760-764. (c) Formyl-acylal **20**: DeBoer, A.; Ellwanger, R. E. *J. Org. Chem.* **1974**, *39*, 77-83.



- A similar mechanistic rationale was proposed to explain formation of mixed acylals **19** and **20**; See refs 14b-c for details.
- Nudelman, A.; Levovich, I.; Cutts, S. M.; Phillips, D. R.; Rephaeli, A. *J. Med. Chem.* **2005**, *48*, 1042-1054.
- Su, W.; Can, J. *J. Chem. Res.* **2005**, 88-90.
- Formyl-acylals have been prepared previously in moderate 44-57% yields via reaction of aldehydes with an acid anhydride and formic acid in the presence of phosphorus pentoxide, see: Scheeren, J. W.; Tax, W. J. M.; Schijf, R. *Synthesis* **1973**, 151-153.
- For other *N*-formylation reactions in water see: (a) Habibi, D.; Sahebkhietari, H.; Nasrollahzadeh, M.; Taghipour, A. *Lett. Org. Chem.* **2013**, *10*, 209-212. (b) Kaboudin, B.; Khodamorady, M. *Synlett* **2010**, 2905-2907.
- For other non-catalyzed solvent-free *N*-formylation reactions, see: (a) Rahman, M.; Kundu, D.; Hajra, A.; Majee, A. *Tetrahedron Lett.* **2010**, *51*, 2896-2899. (b) Habibi, D.; Nasrollahzadeh, M. *Compt. Rend. Chim.* **2013**, *16*, 1008-1016. (c) Dhake, K. P.; Tambade, P. J.; Singhal, R. S.; Bhanage, B. M. *Green Chem. Lett. Rev.* **2011**, *4*, 151-157. (d) Lebleu, T.; Kotsuki, H.; Maddaluno, J.; Legros, J. *Tetrahedron Lett.*, **2014**, *55*, 362-364. (e) Batuta, S.; Begum, N. A. *Synth. Comm.* **2017**, *47*, 137-147.
- (a) Nishikawa, Y.; Nakamura, H.; Ukai, N.; Adachi, W.; Hara, O. *Tetrahedron Lett.* **2017**, *58*, 860-863. (b) El-Dine, T. M.; Evans, D.; Rouden, J.; Blanchet, J. *Chem. Eur. J.* **2016**, *22*, 5894-5898. (c) Hill, D. R.; Hsiao, C. N.; Kurukuluriya, R.; Wittenberger, S. J. *Org. Lett.* **2002**, *4*, 111-113. (d) Suchy, M.; Elmehriki, A. A. H.; Hudson, R. H. E. *Org. Lett.* **2011**, *13*, 3952-3955. (e) Duczek, W.; Deutsch, J.; Vieth, S.; Niclas, H. J. *Synthesis* **1996**, 37-38. (f) Kisfaludy, L.; Otvos, L. *Synthesis* **1987**, 510. (g) Kim, J.-G.; Jang, D. O. *Synlett* **2010**, 1231-1234. (h) Chancellor, T.; Morton, C. *Synthesis* **1994**, 1023-1025.
- (a) Fayol, A.; Housseman, C.; Sun, X. W.; Janvier, P.; Bienaymé, H.; Zhu, J. P. *Synthesis* **2005**, 161-165. (b) Yang, P.-Y.; Liu, K.; Ngai, M.-H.; Lear, M. J.; Wenk, M. R.; Yao, S. Q. *J. Am. Chem. Soc.* **2010**, *132*, 656-666. (c) Fukuda, T.; Wagatsuma, H.; Kominami, Y.; Nogata, Y.; Yoshimura, E.; Chiba, K.; Kitano, Y.

- Chem. Biodiv.* **2016**, *13*, 1502-1510. (d) Soriano-Maldonado, P.; Rodriguez-Alonso, M. J.; Hernandez-Cervantes, C.; Rodriguez-Garcia, I.; Clemente-Jimenez, J. M.; Rodriguez-Vico, F.; Martinez-Rodriguez, S.; Las Heras-Vazquez, F. J. *Process Biochem.* **2014**, *49*, 1281-1287.
23. Aleiwi, B. A.; Mitachi, K.; Kurosu, M. *Tetrahedron Lett.* **2013**, *54*, 2077-2081.
24. Yang, K. H.; Fang, H.; Ye, J. S.; Gong, J. Z.; Wang, J. T.; Xu, W. F. *Pharmazie* **2008**, *63*, 779-783.